

# Epinephrine Hand Nebulizer in Asthma

## Technique of Use, Clinical Aspects

A. M. TARGOW, Ph.D., M.D., *Los Angeles*

### SUMMARY

*It behooves the physician seeking relief for asthmatic patients not to be casual about the epinephrine hand nebulizer and the manner in which it is used. Patients who claim to get no relief from the nebulizer should be asked to demonstrate their technique. If the nebulizer produces a hardly visible mist, it should be discarded. For many patients, the goal in spraying by hand must be the production of more or less continuous and voluminous aerosol, regardless of the phase of respiration, in order to effect relief. If the respiratory pattern has not deviated too far from normal in rate and depth, inhalations may be carried out in courses or cycles of about a half-minute duration and spaced a few minutes apart. If the respiratory pattern is abnormal during the act of spraying, it must be corrected.*

*Inhaled epinephrine aerosols as constituted today appear to be somewhat irritating to the mouth, throat, and upper portion of the pulmonary tract of some persons, but it has not been convincingly demonstrated that serious and permanent damage to the lower respiratory tract of humans can occur from long-continued use of inhaled epinephrine.*

ALTHOUGH the general procedure involved in using the epinephrine hand nebulizer is readily grasped by the average patient, the actual performance in many instances leaves much to be desired. Physicians for the most part assume that patients will acquire proficiency either from experience or from the printed directions accompanying the instruments when purchased. However, the latter source of information is frequently far from adequate and most patients are fearful of self-experiment with such a potent drug. The result is that many an asthmatic patient fails to obtain relief solely because of poor technique, a fact pointed out by one of the popularizers<sup>5</sup> of this method of therapy. Despite this situation, no detailed discussion of the technique of use of the hand nebulizer has appeared in the literature.

Recent interest on the part of investigators in the development of other devices<sup>8, 9, 14</sup> for producing inhalant materials may possibly soon lead to obso-

lescence of the epinephrine hand bulb nebulizer. Until such time as this occurs the present communication may prove to be helpful to the practitioner who sees only an occasional asthmatic patient and may therefore not be aware that pitfalls in the technique of use of the hand nebulizer can unnecessarily rob certain patients of relief.

What follows does not apply either to patients in status asthmaticus or to those who respond so readily to one or two inhalations that they absorb an adequate amount no matter how they use the nebulizer. It pertains rather to a considerable group of patients who fall between these two extremes, who are generally ambulatory but subject to asthmatic seizures of moderate to severe intensity and of variable frequency, and in whom the difference between success and failure in obtaining relief by inhalation depends on inhaling a certain minimal quantity within a relatively short period of time.

The commonest error committed by patients in this group is to attempt to synchronize inspiration with manual compression of the bulb. This error is furthered by the many vendors who sell the nebulizers packaged with their own particular trade name for what is essentially a 1:100 solution of epinephrine hydrochloride. Typical directions in such a package instruct the patient: "Hold the nebulizer outlet inside the mouth, and with mouth open squeeze the bulb while inhaling. Do not pump while exhaling. Only a few inhalations are necessary. If symptoms are not relieved in a few minutes, the inhalations may be repeated." What usually happens in following such directions is that the patient begins to inspire so far in advance of compression of the bulb that inspiration is almost completed before any epinephrine enters the lungs. For the patients under discussion here a larger intake than can ever be obtained by this method is necessary.

Since the aim of therapy is to produce relief, not to economize on epinephrine, it is advisable at all times to keep the mouth of the patient so full of the aerosol that the material can be readily sucked down into the lungs from the very beginning of inspiration. This can be accomplished only by rapidly repeated forcible compressions of the bulb, regardless of the phase of respiration. In this way, the conditions of constant flow obtained by attaching the nebulizer to an oxygen tank are approximated.

If the respiratory pattern has not deviated too far from normal in rate and depth, the patient may inhale a considerable number of times before he stops spraying. Comparative freedom from side-effects is one of the advantages offered by this route of ad-

From the Division of Allergy, Department of Medicine, University of Southern California School of Medicine, Los Angeles.

ministration. However, a method of minimizing inhalation of needless excess is to caution the patient not to inhale more than ten to twelve times, or for longer than a half minute at a time, then to wait for a few minutes to see what degree of relief will ensue before repeating the course of inhalations. As many as five or six successive half-minute courses, spaced a few minutes apart, may then be attempted before it can be concluded that relief by this method is not obtainable.

The degree of relief attained by this technique will be found to run a gamut from complete relief after a few initial inhalations to only partial relief or no relief even after six courses or more. For those who respond slowly, the later courses may bring about a greater degree of relief than the first or second, but the degree of relief is as a rule maximal after five or six periods of inhalation, so that if relief is at this time only partial or absent, further spraying is generally useless for the time being.

Many patients unconsciously alter their breathing pattern when nebulizing. Some, on the one hand, will exaggerate both rate and depth of respiration. Patients in this group who cannot be taught to approximate the normal must be cautioned to restrict themselves to no more than three or four exaggerated respiratory excursions at a time during each course lest symptoms of hyperventilation develop. Other patients, on the other hand, will unaccountably diminish respiratory excursions to a notable shallowness, almost holding the breath while spraying. Patients in this group should be taught either to convert to a normal rate and depth or to adopt the pattern of a few forced, exaggerated respirations per spraying cycle as in the preceding group.

Some persons find it almost impossible at first to avoid synchronizing nebulization with inspiration. They apparently lack a ready facility to carry on a hand compression of the bulb as a separate act by itself at a rate different from the respiratory rate. In these circumstances it is best for some other member of the family to work the hand bulb until such time as the patient can learn to do this properly for himself.

#### FAULTY INSTRUMENTS

In spite of close attention to the preceding details relative to the respiratory pattern, failure may yet ensue if the nebulizer is not an efficient one. It is unfortunate that one instrument which is designated as a vaporizer and is widely sold today under the name of a nationally known pharmaceutical house delivers a mist so meager in volume that a high percentage of patients, in the author's experience, fail to obtain relief with it. This is in accord with the similar experience of Harsh<sup>7</sup> with this instrument. Patients using this model who are certain they cannot obtain relief from inhaled epinephrine are agreeably suprised with results obtained with a nebulizer producing a more voluminous mist.

#### EFFECT ON MUCOSA

Since what is being advocated here is the liberal use of nebulized epinephrine during an asthmatic paroxysm to ensure that maximum benefit may be attained, the question of injury to the respiratory mucosa arises.

Injury has been experimentally produced in animals by long-continued exposure to epinephrine mist. Fox<sup>3</sup> sprayed rabbits intranasally with a 1:1,000 solution of epinephrine hydrochloride over a three-month period and on sectioning the maxilloturbinate found that the mucosa showed increased leukocytic infiltration with formation of intra-epithelial abscesses and areas of denudation of the epithelium. Galgiani<sup>4</sup> and co-workers used the 1:100 dilution as a spray for a few months in cats and rabbits. In some of the animals, but not all, loss of tracheal cilia and desquamation of the tracheal and bronchial epithelium with inflammatory changes in the sub-mucosa were noted. In one human subject moribund from tuberculosis and subjected to frequent spraying in the 48-hour period before death, similar changes were demonstrable postmortem and were attributed to the epinephrine.

It is curious, however, that despite widespread use of the nebulizer since its popularization<sup>6,11</sup> some years ago, severe injury of the lower respiratory tract due to frequent inhalation has not been reported in humans save very recently by Benson and Perlman.<sup>2</sup> These observers reported a few cases in which they felt that death had been caused by excessive use of 1:100 epinephrine for relief of asthma. They postulated a sequence of events in these instances whereby damage to the respiratory mucosa became severe enough to lead to infection with subsequent formation of occluding plugs, anoxia, and death. Unfortunately for their thesis, and as the authors themselves admit, the pathological changes they describe (loss of cilia, epithelial metaplasia and desquamation, cellular infiltration of the sub-epithelial layers) were described at postmortem examination of asthmatics before the era of epinephrine inhalation. To ascribe these changes to epinephrine and to claim an increased mortality therefrom is at variance with the experience of observers<sup>5,12,13</sup> who have administered aerosolized epinephrine to innumerable patients without any seeming ill effects, or at any rate without any effects that have hitherto been ascribed to inhalation therapy. Benson and Perlman believe that the pulmonary changes in question constitute a pattern of injury reproducible by any irritant and the occurrence of this pattern in asthmatic patients before the widespread use of epinephrine inhalation cannot discredit the role of the drug in the production of such changes also.

It cannot be denied that some degree of irritation does occur in the mouth and throat in a fairly high percentage of patients.<sup>5,6,10</sup> Patients frequently complain of dryness and/or burning in the throat area following even short-time use of the spray. Transient

mild irritation of the lower bronchial tree may also be a factor in the initial increase in coughing which follows immediately after inhalation in many instances, and which is quite helpful in dislodging and bringing up mucus. (It should be kept in mind, however, that later bouts of coughing may be due to stimulation of sensory nerve endings by loosened plugs of mucus. It is well, incidentally, to caution patients that a pinkish stain which may appear in material that is coughed up is due to oxidation of the epinephrine and not, as many frightened patients assume, to blood. The possibility of hemoptysis must nevertheless always be kept in mind and in case of doubt appropriate procedures instituted to ascertain the nature of the stain.)

#### MINIMIZING IRRITATION

One simple method of minimizing irritation is to direct the patient to rinse the mouth after each session of spraying.<sup>6</sup> Lockey<sup>10</sup> pointed out that irritation may also be minimized by adding glycerine to the epinephrine solution to a final concentration of 5 per cent. Other advantages accruing from glycerine, such as stabilization of the particle size of the mist, have been pointed out by Abramson,<sup>1</sup> who favors a 25 per cent concentration, and concurred in by Harsh<sup>7</sup> who pointed out still further advantages such as a bacteriostatic and a wetting effect.

In most instances any irritation produced by the aerosol is transient and subsides either because the interval between asthmatic seizures is sufficiently long, or because the average patient with localized symptoms of any severity will desist from further use of the nebulizer until the symptoms have disappeared. There is thus a distinct difference between humans who naturally bring their defense mechanisms into play and animals who are not permitted to do so, as in the experiments mentioned. Also, species and individual differences may be of importance, since every allergist encounters patients who use unbelievably large quantities of epinephrine by inhalation and by injection daily for months and years without any apparent ill effects.

In certain instances, however, asthma is persistent enough, and severe enough, so that the temptation to continued use despite symptoms of irritation is overwhelming. It is in these instances that the possibility may arise of serious damage to the lower respiratory tract from long-continued inhalation. In such circumstances, if the nebulizer is only minimally effective it may be simple enough to prohibit its use and substitute other measures of equal or greater efficacy. Some patients in fact learn by experience that the spray suffices only for the milder attacks and automatically discard it for other measures for the more severe attacks.

The advantages of this method of therapy are ease of application, quickness of response, comparative freedom from side-reactions, and, to a degree depending on the severity of the asthma, comparative freedom from home confinement by reason of portability of the nebulizer. Many a patient's life has

been made bearable through the use of this simple contrivance. Given such a situation—but provided, of course, that similar relief cannot be obtained in any other way—the propriety of denying to the patient the benefits of inhaled epinephrine is open to question. One must look askance at a logic which attaches utmost importance to protection of the respiratory tract from possible permanent damage which might accrue over a long period of time and precludes all consideration of the patient's general comfort and well-being from day to day. In this connection the recently expressed opinion of an asthmatic patient who is himself a physician<sup>15</sup> is illuminating: "Not being able to see my bronchial mucosa I am not worried about [the effect of the spray on] its possible thickness or the inactivity of its cilia. I am, however, able to carry out a full day's work. . . . If my life has been shortened by using adrenaline sprays, at least I shall have had more hours of useful activity on earth than I should otherwise have had."

It would seem, then, that with respect to this problem of long continued use of the hand nebulizer there is at present no substitute for the exercise of judgment by the physician in each individual instance. One comes thus to the same conclusion as did Galgiani<sup>4</sup> and his co-workers who despite the results of their animal experimentation and despite being convinced that considerable local damage may result stated: "The clinician would therefore seem to be under the necessity of deciding in each individual case whether the gain in convenience of medication by inhalation is great enough to justify the possible production of added pathologic changes."

#### OTHER DISADVANTAGES OF USE OF HAND NEBULIZER

It is necessary to point out that damage to the respiratory tract is not the only objection that can be advanced against the use of the nebulizer. There is a measure of correctness in the view held by some allergists that if an asthmatic patient gets satisfactory relief by this method without ever having gone to a physician, or shortly after he is introduced to this technique by a physician, he may stay away from medical observation and thus the cause of the asthma may never be determined. This possibility is enhanced by the present widespread and unregulated over-the-counter traffic in the sale of both nebulizers and solution. If the onset of asthma is in adult life, and symptoms remain moderate in degree without leading to organic changes in the cardiopulmonary apparatus, the matter may be of no consequence. In the case of a child, however, failure to seek proper medical care may lead to undesirable consequences.

It is true, furthermore, that some patients use the nebulizer with unnecessary frequency, at the slightest sensation of "pressure" or "heaviness" in the chest, without waiting to see whether or not their symptoms will subside. Such patients may build up a neurotic dependence upon having the nebulizer ever

at hand. Illustrative of an interesting psychosomatic aspect of asthma, it is conceivable that a few individuals in this group may at times develop asthma solely as a fear-conditioned reflex should they perchance unexpectedly find themselves without the nebulizer in their possession. Some physicians, for any or all of these reasons, refuse to allow their patients to use a nebulizer. But the solution of these problems should not lie in interdicting the use of the nebulizer by those who desperately need it merely because some may use it unwisely and without supervision.

6333 Wilshire Boulevard.

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